Amyloid-beta Induced Sleep Fragmentation is Rescued by Fatty-acid Binding Proteins in *Drosophila*

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Sleep amount and quality are known to decline with age. This effect is even more pronounced in Alzheimer's disease (AD), and is a major contributing factor for institutionalization. Amyloid-beta (Aβ) aggregation increases during AD, and is associated with disruption of sleep. Sleep/wake disturbances may also accelerate the neurodegenerative process. Therefore, identifying changes in sleep prior to clinical onset may serve as a prodromal marker to facilitate interventions that delay AD progression. Molecular mechanisms which contribute to disturbed sleep in AD are not known and therefore present a challenge for development of therapeutic strategies. Fatty-acid binding proteins (Fabp) are small chaperones that shuttle long-chain fatty-acids such as docosahexaenoic acid, a lipid known to reduce Aβ plaque burden and restore cognitive deficits in AD mouse models. Fabp expression cycles based on time-of-day, has been implicated sleep and memory processes, and is reduced at synapses following aging. Transgenic flies which express Aβ are syndromal to human AD, and have progressive cognitive deficits and neurodegeneration. Here, we were interested in characterizing the effects of Fabp expression on sleep in a Drosophila AD model. Flies carrying a transgene that induces the expression of human Aβ42 peptide under the control of a neuronal promoter were examined for changes in sleep using a video monitoring assay. Aβ42-flies sleep was compared with control flies with or without the presence of another transgene that overexpresses the Drosophila Fabp gene. We observed Aβ flies have significantly reduced sleep in both daytime and night-time at ages which precede memory loss and neurodegeneration. The reduction in sleep observed in Aβ flies is rescued with flies that carry a Drosophila Fabp transgene. These data suggest that sleep can serve as a prodromal marker in an AD animal model, and that Fabp may be a novel therapeutic target for the treatment of AD symptoms.

Trainee Award Eligible